In the Specification:

Please amend the specification as shown:

Please delete the paragraph on page 27, lines 13-17, and replace it with the following paragraph:

FIGURE 5. E1A inhibits Tcf-dependent transcription. (A) Schematic diagram of the E1A12S mutants **(SEQ ID NOS 63, 64, 64, 65 & 66, respectively in order of appearance)**. (B-D) Luciferase assays with a wild-type E2 reporter and Tcf-E2 reporters. The "Tcf-E2 mut E3" reporter contains inactivating mutations in the E3 enhancer (9). Cells were transfected with luciferase reporters and plasmids expressing E1A mutants (shown in A). (B) SW480, (C) Co115, (D) Hct116.

Please delete the paragraph on page 28, lines 11-12, and replace it with the following paragraph:

FIGURE 9. Comparison of sequences of wild type Ad5 E1A promoter **(SEQ ID NO: 27)** and Tcf mutation E1A promoter **(SEQ ID NO: 47)** of the present invention.

Please delete the paragraph on page 28, lines 14-15, and replace it with the following paragraph:

FIGURE 10. Comparison of sequences of wild type AD5 E4 promoter **(SEQ ID NO: 28)** and Tcf mutation E4 promoter **(SEQ ID NO: 29)** of the present invention.

Please delete the paragraph on page 30, lines 11-28, and replace it with the following paragraph:

Primers

GGGTGGAAAGCCAGCCTCGTG (oCF1) **(SEQ ID NO: 2)**

ACCCGCAGGCGTAGAGACAAC (oCF2) **(SEQ ID NO: 3)**

AGATCAAAGGGattaAGATCAAAGGGccaccacctcattat (oCF3) **(SEQ ID NO: 4)**

tCCCTTTGATCTccaaCCCTTTGATCTagtcctatttatacccggtga (oCF4) **(SEQ ID NO: 5)**
tCCCTTTGATCTccactagtgtgaattgtagttttcttaaaatg (oCF5) **(SEQ ID NO: 6)**
GAACTAGTAGTAAATTTGGG CGTAACC (oCF6) **(SEQ ID NO: 7)**
ACGCTAGCAAAACACCTGGGCGAGT (oCF7) **(SEQ ID NO: 8)**
CATTTTCAGTCCC GGTGTCG (oCF8) **(SEQ ID NO: 9)**
ACCGAAGAAATGGCCGCCAG (oCF9) **(SEQ ID NO: 10)**
TCTGTAATGTTGGCGGTGCAGGAAG (oCF10) **(SEQ ID NO: 11)**
ATGGCTAGGAGGTGGAAGAT (oCF12) **(SEQ ID NO: 12)**
and GTGTCGGAGCGGCTCGGAGG (oCF13) **(SEQ ID NO: 13)**
CAGGTCCTCATATAGCAAAGC (IR213 E1A antisense) **(SEQ ID NO: 14)**
TGTCTGAACCTGAGCCTGAG) (IR190 E1B sense) **(SEQ ID NO: 15)**
CATCTCTACAGCCCATAC (IR110 E2/E3 sense) **(SEQ ID NO: 16)**
AGTTGCTCTGCCTCTCCAC (IF171 E2/E3 antisense) **(SEQ ID NO: 17)**
CGTGATTAAAAAGCACCACC (IR215 E4 sense) **(SEQ ID NO: 18)**

Please delete the paragraph on page 31, line 1 to page 32, line 4, and replace it with the following paragraph:

Previously disclosed (Wo 00/56909) primers

G61 5'-TGCATTGGTACCGTCATCTCTA-3' **(SEQ ID NO: 30)** Ad 5, 26688 (E2 region)

G62 5'-GTTGCTCTGCCTCTCCACTT-3' **(SEQ ID NO: 31)** Ad 5, 27882 (E2 region)

G63 5'-CAGATCAAAGGGATTAAGATCAAAGGGCCATTATGAGCAAG-3' **(SEQ ID NO: 32)**
iPCR, E2 promoter replacement (2 x Tcf), upper primer

G64 5'-GATCCCTTTGATCTCCAACCCTTTGATCTAGTCCTTAAGAGTC-3' **(SEQ ID NO: 33)**
iPCR, E2 promoter replacement (2 x Tcf), lower primer

G74 5'-GGG CGA GTC TCC ACG TAA ACG-3' **(SEQ ID NO: 34)**
Ad5, 390 (left arm gap repair fragment)

G75 5'-GGG CAC CAG CTC AAT CAG TCA-3' **(SEQ ID NO: 35)**
Ad5, 36581 (right arm gap repair fragment)

G76 5'-CGG AAT TCA AGC TTA ATT AAC ATC ATC AAT AAT ATA CC-3' **(SEQ ID NO: 36)**
Ad5 ITR plus EcoRI, HindIII and PacI sites

G77 5'-GCG GCT AGC CAC CAT GGA GCG AAG AAA CCC A-3' **(SEQ ID NO: 37)**
Ad 5, 2020 (E1B fragment plus NheI site)

G78 5'-GCC ACC GGT ACA ACA TTC ATT-3' **(SEQ ID NO: 38)**
Ad 5, 2261 (E1B fragment plus AgeI site)

G87 5'-AGCTGGGCTCTCTTGGTACACCAGTGCAGCGGGCCAACTA-3' **(SEQ ID NO: 39)**
iPCR to destroy the E3 NF-1, L1 and L2 binding sites, upper primer

G88 5'-CCCACCACTGTAGTGCTGCCAAGAGACGCCCAGGCCGAAGTT-3' **(SEQ ID NO: 40)**
iPCR to destroy the E3 NF-1, L1 and L2 binding sites, lower primer

G89 5'-CTGCGCCCCGCTATTGGTCATCTGAACTTCGGCCTG-3' **(SEQ ID NO: 41)**
iPCR to destroy the E3 ATF and AP-1 binding sites, upper primer

G90 5'-CTTGCGGGCGGCTTTAGACACAGGGTGCGGTC-3' **(SEQ ID NO: 42)**
iPCR to destroy the E3 ATF and AP-1 binding sites, lower primer

G91 5'-CAGATCAAAGGGCCATTATGAGCAAG-3' **(SEQ ID NO: 43)**
iPCR, E2 promoter replacement (1 x Tcf), upper primer

G92 5'-GATCCCTTTGATCTAGTCCTTAAGAGTC-3' **(SEQ ID NO: 44)**
iPCR, E2 promoter replacement (1 x Tcf), lower primer

G100 5'-ATGGCACAAACTCCTCAATAA-3' **(SEQ ID NO: 45)**
Ad 5, 27757 (E3 distal promoter region)

G101 5'-CCAAGACTACTCAACCCGAATA-3' **(SEQ ID NO: 46)**
Ad 5, 27245 (E3 distal promoter region)

Please delete the paragraph on page 32, lines 6-9, and replace it with the following paragraph:

Mutant leftITR and E1A promoter

catcatcaataatataccttattttggattgaagccaatatgataatgaggTggtggCCCTTT
GATCTTAATCCCTTTGATCTGGATCCCTTTGATCTCCAACCCTTTGATCTAGTCCtatttata
(SEQ ID NO: 19),

Please delete the paragraph on page 32, lines 12-22, and replace it with the following paragraph:

Adenovirus mutagenesis

An Ad5 E1A fragment (nucleotides nt 1 to 952) was amplified by PCR from ATCC VR5 adenovirus 5 genomic DNA with primers CGGAATTCAAGCTTAATTAACATCATCAATAATATACC (G76) **(SEQ ID NO: 36)** and GGGTGGAAAGCCAGCCTCGTG (oCF1) **(SEQ ID NO: 2)**, cut with PacI, and cloned into the BamHI/PacI sites in pMB1 (see WO 00/56909 incorporated herein by reference) to give pCF4. pMB1 contains the left end of Ad5 cloned into the EcoRI/SmaI sites of pFL39 (**Bonneaud, N., K. O. Ozier, G. Y. Li, M. Labouesse, S. L. Minvielle, and F. Lacroute.** 1991. Yeast. **7:**609-15 and **Brunori, M., M. Malerba, H. Kashiwazaki, and R. Iggo.** 2001.. J Virol. **75:**2857-65 both incorporated herein by reference.

Please delete the paragraph on page 32, line 23, to page 33, line 4, and replace it with the following paragraph:

The endogenous adenoviral sequence from the middle of the ITR to the E1A TATA box was replaced with four Tcf binding sites by inverse PCR with primers tcc AGATCAAAGGGattaAGATCAAAGGGccaccacctcattat (oCF3) **(SEQ ID NO: 4)** and tCCCTTTGATCTccaaCCCTTTGATCTagtcctatttatacccggtga (oCF4) **(SEQ ID NO: 5)** to give pCF25 (the Tcf sites in the primers are shown in capitals). The final sequence of the mutant ITR and E1A promoter is catcatcaataatataccttattttggattgaagccaatatgataatgaggTggtggCCCTTT GATCTTAATCCCTTTGATCTGGATCCCTTTGATCTCCAACCCTTTGATCTAGTCCtatttata **(SEQ ID NO: 19)**, where the wt Ad5 sequence is in lowercase and the E1A TATA box is underlined. A G to T mutation was introduced just before the first Tcf binding site to mutate the Sp1 binding site (**Leza, M. A., and P. Hearing.** 1988J Virol. **62:**3003-13 incorporated herein by reference).

Please delete the paragraph on page 33, lines 5-16, and replace it with the following paragraph:

The Ad5 E4 fragment (nt 35369 to 35938) was amplified by PCR from VR5 DNA with primers G76 and ACCCGCAGGCGTAGAGACAAC (oCF2) **(SEQ ID NO: 3)**, cut with PacI and cloned into the BamHI/PacI sites in pMB1 to give pCF6. To compensate for the mutations introduced in the left ITR, three Tcf binding sites were introduced, and the endogenous sequence (nt 35805 to 35887) was simultaneously deleted by inverse PCR with primers oCF3 and tCCCTTTGATCTccactagtgtgaattgtagttttcttaaaatg (oCF5) **(SEQ ID NO: 6)** to give pCF16 (the Tcf site is shown in capitals and the SpeI site is underlined). The packaging signal was amplified by PCR from pCF6 with primers GAACTAGTAGTAAATTTGGG CGTAACC (oCF6) **(SEQ ID NO: 7)** and ACGCTAGCAAAACACCTGGGCGAGT (oCF7) **(SEQ ID NO: 8)**, cut with SpeI/NheI and cloned into the SpeI site in pCF6 to give pCF34. The packaging signal has the same end-to-center orientation as at the left end of the adenoviral genome.

Please delete the paragraph on page 33, lines 17-22, and replace it with the following paragraph:

The Δ2-11 mutation was introduced in two steps. First, plasmids pCF4 (wild type E1A promoter) and pCF25 (Tcf-E1A mutant) were cut by SnaBI/SphI following by self ligation to give pRDI-283 and pRDI-284, respectively. Second, the 2-11 region in pRDI-283 and pRDI-284 was deleted by inverse PCR with primers CATTTTCAGTCCC GGTGTCG (oCF8) **(SEQ ID NO: 9)** and ACCGAAGAAATGGCCGCCAG (oCF9) **(SEQ ID NO: 10)** to give pCF61 and pCF56, respectively.

Please delete the paragraph on page 34, line 17, through page 35, line 2, and replace it with the following paragraph:

Viral genomic DNA was converted into virus by transfection of PacI digested YAC/BAC DNA into cR1 cells. The viruses were then plaque purified on SW480 cells, expanded on SW480, purified by CsCl banding, buffer exchanged using NAP25 columns into 1 M NaCl, 100 mM Tris-HCl pH 8.0, 10% glycerol and stored frozen at -70°C. The identity of each batch was checked by restriction digestion and automated fluorescent sequencing on a Licor 4200L sequencer in the E1A (nt 1-1050), E1B (nt 1300-2300), E2/E3 (nt 26700-27950) and E4 (nt 35250-35938) regions using primers IR213 (E1A antisense:

CAGGTCCTCATATAGCAAAGC) **(SEQ ID NO: 14)**, IR190 (E1B sense: TGTCTGAACCTGAGCCTGAG) **(SEQ ID NO: 15)**, IR110 (E2/E3 sense: CATCTCTACAGCCCATAC) **(SEQ ID NO: 16)**, IF171 (E2/E3 antisense: AGTTGCTCTGCCTCTCCAC) **(SEQ ID NO: 17)** and IR215 (E4 sense: CGTGATTAAAAAGCACCACC) **(SEQ ID NO: 18)**. Apart from the desired mutations, no differences were found between the sequence of VR5 and the Tcf viruses. Particle counts were based on the OD_{260} of virus in 0.1% SDS using the formula 1 $OD_{260} = 10^{12}$ particles/ml.

Please delete the paragraph on page 35, lines 4-17, and replace it with the following paragraph:

E1A, p300, P/CAF, Tip49 and β-catenin plasmids

Wild type 12S E1A (pCF9) and E1A mutants ΔpRb (124A,135A), Δp300N (Δ2-11), Δp300C (Δ64-68), Δp400 (Δ26-35), ΔP/CAF (E55), ΔCtBP (LDLA4), and ΔC52 have been described by Alevizopoulos et al (1998) EMBO J. **17:**5987-97 and Alevizopoulos et al. (2000) Oncogene. **19:**2067-74 and Reid et al. (1998) EMBO J. **17:**4469-77 all incorporated herein by reference. All the mutants were provided in a pcDNA3 backbone (Invitrogen, Carlsbad, USA) except the Δp300N and Δp300C mutants that were isolated with BamHI/EcoRI and cloned into the BamHI/EcoRI sites of pcDNA3. The ΔCR1 mutant (Δ38-68) was made by inverse PCR of pCF9 with primers TCTGTAATGTTGGCGGTGCAGGAAG (oCF10) **(SEQ ID NO: 11)** and ATGGCTAGGAGGTGGAAGAT (oCF12) **(SEQ ID NO: 12)** to give pCF45. The ΔΔ p300-P/CAF double mutant was constructed by three way ligation of BstXI fragments from the single mutants. The ΔN-ß-catenin plasmid has been described by Van de Wetering et al. 1997. Cell. **88:**789-99 (incorporated herein by reference).

Please delete the paragraph on page 36, lines 11-26, and replace it with the following paragraph:

Luciferase assays

The E2 reporters were described below. To construct E1A reporters, wild type and mutant E1A promoters were amplified by PCR from pCF4 and pCF25, respectively, with primers G76 and GTGTCGGAGCGGCTCGGAGG (oCF13) **(SEQ ID NO: 13)**, cut with HindIII, and cloned into the NcoI/HindIII sites of pGL3-Basic (Promega, Madison, USA). Cells were seeded at $2.5x10^5$ cells per 35-mm well 24 hours before transfection. 4.5 μl of Lipofectamine (Invitrogen, Carlsbad, USA) was mixed for 30 minutes with 100 ng of reporter plasmid, 1 ng of control Renilla luciferase plasmid (Promega, Madison, USA) and 500 ng of vectors expressing E1A, P/CAF, p300 or TIP49. pcDNA3 empty vector was added to equalise the total amount of DNA. In figure 5b, 0.5, 1 and 2 μg of p300 vector were used. Cells were harvested 48 hours after transfection and dual luciferase reporter assays performed according to the manufacturer's instructions (Promega, Madison, USA) using a LUMAC Biocounter (MBV). Each value is the mean of one to nine independent experiments done in triplicate and transfection efficiency is normalised to the activity of the Renilla control.

Please delete the paragraphs on page 51, line 27, through page 52, line 3, and replace it with the following paragraph:

Adenovirus mutagenesis

The fibre region (nucleotides nt 30470 to 33598) of adenovirus 5 (ATCC VR5) was cut with KpnI/XbaI and cloned into pUC19 to give pCF159. A SpeI site was inserted after the polyA site of the fibre by inverse PCR with primers AGTTTCTTTATTCTTGGGCAATGT (oCF67) **(SEQ ID NO: 48)** and AGTCGTTTGTGTTATGTTTCAAC (oCF68) **(SEQ ID NO: 49)** to give pCF277.

Please delete the paragraphs on page 52, line 4-8, and replace it with the following paragraph:

yCD was cloned from S.cerevisiae genomic DNA by PCR with primers TCGCTAGCCAGGCACAATCTTCGCATTTCTTTTTTTCCAGATGGTGACAGGGGGAATG GC (oCF31) **(SEQ ID NO: 50)** and TGACTAGTTATTCACCAATATCTTCAAA (oCF32)

(SEQ ID NO: 51). The product was cut with NheI and SpeI (underlined) and inserted into the XbaI site of pyCDNA3 (Invitrogen, Carlsbad, USA) to give pCF232.

Please delete the paragraphs on page 52, lines 9-28, and replace it with the following paragraph:

The EMCV internal ribosome entry site (IRES) was cloned by PCR from the pSE280-IRES plasmid (gift of O. Zillian, ISREC). This plasmid contains the EMCV IRES of pCITE-1 (Novagen, Madison, USA) cut with EcoRI and BalI and cloned into the EcoRI/SmaI sites of pSE280 (Invitrogen, Carlsbad, USA). The IRES was amplified with primers ATGCTAGCGAATTCCGCCCCTCTC (oCF69) **(SEQ ID NO: 52)** and ATACTAGTTATGCATATTATCATCGTGTTT (oCF70) **(SEQ ID NO: 53)**, cut with NheI and SpeI (underlined) and inserted into the SpeI engineered immediately downstream of the fibre to give pCF274. This plasmid contains the full-length wild-type fibre followed by the EMCV IRES. The BfrBI site at the end of the IRES (bold) can be used to introduce a foreign gene, whose first codon is the ATG of the BfrBI site. The polyA site of fibre is embedded at the end of the coding sequence and was mutated by silent mutations (GAA TAA A to GAG TAG A, where the coding sequence remains Glu-Stop). To do so, the 5'-end of the fibre gene was amplified by PCR from pCF274 using primers GGAATTCGCTAGTTTCTCTACTCTTGGGCAATGTA (oCF77, contains the mutant polyA signal, underlined) **(SEQ ID NO: 54)** and GGTGGTGGAGATGCTAAACTCACTTTGGTC (oKH9) **(SEQ ID NO: 55)** and re-introduced into pCF274 using EcoRI and BstXI. The vector obtained after backcloning is pCF328. It contains the full-length wild-type fibre sequence with a mutant polyA site followed by the EMCV IRES. This viral sequence is in a pRS406 backbone, see Gagnebin J et al. Gene Ther 1999; 6: 1742-1750.

Please delete the paragraphs on page 52, line 29, through page 53, line 6, and replace it with the following paragraph:

yCD was cloned by PCR with primers GTGACAGGGGGAATGGCAAG (oCF71) **(SEQ ID NO: 56)** and TGACTAGTTTATTCACCAATATCTTCAAA (oCF76) **(SEQ ID NO: 57)**, cut with SpeI and inserted into the BfrBI/SpeI sites of pCF278, a K7-fibre but otherwise identical derivative of pCF274, to give pCF308. An extra A (bold) was added at the end of yCD (last two codons underlined) to create a polyA signal. The junction between the IRES

and yCD was corrected by PCR to give pCF317. The IRES-yCD cassette of pCF317 was backcloned with AvrII and SpeI into pCF328 to obtain pCF330, the corresponding shuttle vector.

Please delete the paragraphs on page 53, lines 12-17, and replace it with the following paragraph:

The IRES-yCD (pCF330) or splice-yCD (pCF317) sequences were introduced into the vCF11 (A4) YAC/BAC by two-step gene replacement in yeast to obtain vpCF12 and vpCF13, respectively. Plasmids were checked by automated fluorescent sequencing on a Licor 4200L sequencer in the fibre region using primers IF272 (Fibre sense: GCCATTAATGCAGGAGATG) **(SEQ ID NO: 58)** and IR281 (E4 antisense: GGAGAAAGGACTGTGTACTC) **(SEQ ID NO: 59)**.

Please delete the paragraph on page 56, lines 14-23, and replace it with the following paragraph:

RT was performed with oligo-dT12-18 (Amersham Biosciences, Little Chalfont, UK) and Superscript II reverse transcriptase (Invitrogen, Carlsbad, USA) according to the manufacturer's instructions. yCD was amplified with Pfu turbo (Stratagene, La Jolla, USA) using primers oCF76 and AGGATCCACTCTCTTCCGCATCGCTGTC **(SEQ ID NO: 60)** (TPLupper). Bands were purified from a TAE agarose gel and 3' A-Overhangs were added with Taq DNA Polymerase (Sigma, St. Louis, USA). The PCR product was cloned by TOPO TA cloning into pCR2-1-TOPO following the manufacturer's instructions (Invitrogen, Carlsbad, USA) and sequenced using primers AGGGTTTTCCCAGTCACGACGTT **(SEQ ID NO: 61)** (M13fwd) and AGCGGATAACAATTTCACACAGGA **(SEQ ID NO: 62)** (M13rev).

Please delete the paragraph on page 57, lines 9-22, and replace it with the following paragraph:

Promoter replacement sequences inserts for preparing Ad-Tcf viruses
single Tcf site:

ATCAAAGGG **(SEQ ID NO: 20)**

2 Tcf sites:
ATCAAAGGGATCCAGATCAAAGG- **(SEQ ID NO: 21)**

3 Tcf sites:
ATCAAGGGTTGGAGATCAAAGGGATCCAGATCAAAGGGATTAA
GAT CAAAGG- **(SEQ ID NO: 22)**

4 Tcf sites:
-ATCAAAGGGTTGGAGATCAAAGGGATCCAGATCAAAGGGATTA
AGATCAAAGG- **(SEQ ID NO: 23)**